1.1 COMPARISON OF OFF-LINE THREE-DIMENSIONAL AND REAL-TIME TWO-DIMENSIONAL ULTRASOUND ASSESSMENT OF NUCHAL TRANSLUCENCY: A PILOT STUDY OF 100 CASES

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Background: Good levels of correlation between NT assessment by two-dimensional (2D) and transvaginal three-dimensional (3D) ultrasound (US) have been demonstrated,[1,2] but few studies have addressed the reliability and feasibility of transabdominal 3D US.[3] Evidence suggests that real time US to assess nuchal translucency (NT) may not be required in the future as 3D volumes can be stored and analysed off-line.[4]
Objective: To assess the reliability and feasibility of measuring NT in 3D vs 2D using a stored dataset.
Methodology: Prospective study of 100 singleton pregnancies between 11 and 13+6 weeks. NT was measured in 2D according to Fetal Medicine Foundation guidelines. A 3D volume sweep of the entire fetus in mid-sagittal plane was captured, stored on the machine's hard drive and copied to a compact disc. This dataset was analysed off-line on a laptop computer by an independent blinded observer and NT measured. Bland-Altman statistical plots were used to compare results.
Results: NT in 3D was successful in 90% of cases. Obesity and fetal movement contributed to poor 3D image in 10 cases. Mean difference of NT in 2D vs 3D was 0.4 mm (95% limits of agreement between -0.769 and 0.803). Each 3D sweep took approximately 10 seconds. Off-line analysis of 3D images took less than 5 minutes in all cases.
Conclusion: Good feasibility of NT in 3D stored datasets and levels of agreement with conventional 2D US allows widening of the national Downs screening programme by resolving training issues and reducing scan times.

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1.2 EPIDERMAL GROWTH FACTOR INCREASES SYSTEM A TRANSPORT AND ATTENUATES APOPTOSIS IN PLACENTAL EXPLANTS

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Background: Fetal growth restriction (FGR) is associated with altered placental trophoblast cell turnover and decreased activity of the system A amino acid transporter. These phenomena are reproduced by placental culture in hypoxic conditions (1% O_2). We hypothesised that treatment with epidermal growth factor (EGF) would restore normal cell turnover and system A transport in hypoxic conditions.
Methods: Placental villous explants were taken from normal term placentas (n = 12) and cultured in 6% and 1% O_2 for 96 h with or without 100 ng/ml EGF over 48–96 h. Following culture, the activity of system A was assessed as Na-dependent uptake of methyl-aminoisobutyric acid (14C-MeAIB). Culture media was assayed for human chorionic gonadotrophin (hCG) and lactate dehydrogenase (LDH). Apoptosis and proliferation in placental tissue was quantified by cytokeratin M30 and Ki-67 immunostaining, respectively.
Results: System A activity was decreased by 30% following culture in 1% compared to 6% O_2 ($p<0.05$). This was reversed by treatment with EGF, which increased system A activity in explants cultured in 1% O_2 by 37% ($p = 0.01$). Apoptosis was increased two-fold in explants cultured in 1% O_2 compared to 6% ($p<0.05$), and this was partially reversed by EGF ($p<0.05$). Trophoblast proliferation, hCG and LDH release were not altered by treatment with EGF.
Conclusions: System A amino acid transporter activity and apoptosis are adversely affected in placental villous explants in hypoxic conditions. These effects are partially reversible by EGF. These findings suggest a link between trophoblast cell turnover and placental function and suggest a potential role for growth factors in normalising placental indices in FGR.

This project was supported by a grant from the Peel Medical Trust.

1.3 LOCAL OVER-EXPRESSION OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN THE UTERINE ARTERIES RESULTS IN LONG-TERM CHANGES IN UTERINE ARTERY BLOOD FLOW AND VASCULAR REACTIVITY IN THE PREGNANT SHEEP

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Background: Impaired utero-placental perfusion leads to fetal growth restriction (FGR), a challenging obstetric complication associated with high morbidity and mortality. Previously, we showed a significant increase in uterine artery blood flow (UABF) and significant changes in the vascular reactivity of pregnant sheep uterine arteries (UtAs) 4–7 days after adenovirus mediated local over-expression of vascular endothelial growth factor (VEGF). The current study investigated the long-term effects.
Methods: UABF was measured objectively using chronically implanted flow probes placed around both the UtAs (n = 9) of mid-gestation pregnant sheep (90 days of gestation, term = 145 - days). Maternal blood pressure was measured using a carotid artery pressure-sensitive catheter. Baseline UABF and haemodynamic values were recorded for one week. We then injected 5×10^{11} particles of adenovirus encoding either the VEGF-A_{165} gene (Ad.VEGF-A_{165}) or a control non-vasoreactive β-galactosidase gene (Ad.LacZ) into each UtA. UABF and maternal haemodynamics were measured daily until term.
Results: The percentage increase in UABF from baseline in the Ad.VEGF injected UtAs was significantly greater than in the Ad.LacZ injected UtAs (39.57% vs 16.01%, $p<0.05$). In the Ad.VEGF transduced vessels there was a diminished contractile response to Phenylephrine (E_{max} 155.7 ± 13.65 vs E_{max} 180.7 ± 10.39, $p<0.05$) and significantly more vessels were observed in the perivascular adventitia (n = 28, 11.64 vs 8.75, $p<0.05$). There were no significant changes in maternal haemodynamics.
Conclusions: Significant changes in UABF, vascular responses and remodelling occur after local over-expression of VEGF long term. We are investigating whether this effect could be used to increase fetal size in growth restricted fetal guinea pigs, and therefore as a potential therapy for FGR.

1.4 AUDIT OF FIRST TRIMESTER CHORIONIC VILLOUS SAMPLING OUTCOMES: A REGIONAL, POPULATION-BASED STUDY

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A regional network of four centres undertaking chorionic villus sampling (CVS) covers the West Midlands, a birth population of 70 000 per annum.

Routinely collected regional data (cytogenetics, congenital anomaly register, and perinatal deaths) linked to local datasets

from CVS centres have generated a population-based cohort of 1145 procedures (2005–2007). Data items include indication for procedure, needle size, needle insertions, and specimen size. Outcomes of pregnancy up to 28 days post delivery were completed in all cases.

A regional group of all CVS operators monitors activity, performance, and outcomes against national guidelines.[1] Loss rates were generated for singleton pregnancies both as crude and corrected rates, which excludes cases with either structural and/or chromosomal anomalies.

The crude loss rates following procedures were 4.3% (2.9% to 5.7%) within 28 days of the procedure, 5.7% (4.1% to 7.2%) before 24 weeks gestation, and 8.4% (6.5% to 10.3%) up to 7 days postnatally. In the fetus group with ''no anomaly'', these were 1.7% (0.7% to 2.7%), 2.8% (1.5% to 4.1%) and 3.6% (2.1% to 5.1%), respectively. Loss rates are stratified for maternal age, multiple needle insertions, and needle size. Each operator and CVS centre receives feedback on outcomes within their population.

Regional data are generated to inform pre-test counselling including the number of procedures that failed to obtain an adequate sample (0.8%), the proportion of women undergoing CVS for trisomy 21 where other aneuploidy is detected (4.6%), and the proportion of specimens with more than one cell line requiring additional sampling (3.2%).

1.5 METABOLIC CHANGES IN PLASMA AND PLACENTAL VILLOUS EXPLANTS FROM WOMEN WHO DELIVER A SMALL FOR GESTATIONAL AGE BABY

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Small for gestational age (SGA) can have lifelong consequences. Placental hypoxia is implicated in its pathophysiology. Metabolomics is the study of all small-molecule compounds within a biological system. We aimed to examine the metabolomic differences in (a) plasma in early pregnancy (15 weeks) and (b) placental villous explants, between women who develop a SGA baby and normal controls. In this way we hope to significantly aid the understanding of the phenotypic nature of SGA by pinpointing metabolic changes at both a *circulatory* and *placental* level.

In study (a), 60 primigravid women (SGA group) were matched to 60 controls. In study (b), placental explants (n = 9) were cultured for 96 hours in 20%, 6% and 1% O_2 and conditioned culture medium collected. Both sample sets were analysed using ultra performance liquid chromatography (UPLC) mass spectrometry (MS), in order to generate a semi-quantitative metabolite profile for each sample.

In the plasma study, univariate analysis identified 191 ''information rich'' peaks ($p<0.05$) and a multivariate discriminant model predicted an AuROC curve of 0.96. 36 metabolites have been identified belonging predominantly to lipid, fatty acid and amino acid classes, the chemical identity of which will be presented in full. In the placental explants, a number of metabolites were identified as being significantly different ($p<0.05$) under different O_2 tensions for both SGA and controls, confirmed by multivariate analysis.

These results will provide direction for future research to aid the pathophysiological understanding of SGA and early pregnancy plasma differences may form the basis of biomarker screening of SGA.

1.6 HUMAN PRIMARY CYTOTROPHOBLASTS FROM NORMAL AND INTRAUTERINE GROWTH RESTRICTION PREGNANCIES RESPOND DIFFERENTLY TO T3 TREATMENT IN VITRO

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Intrauterine growth restriction (IUGR) is an important cause of perinatal mortality and morbidity. We previously reported lower fetal circulating concentration of thyroid hormones (THs) in severe IUGR compared to gestationally-matched normal fetuses. The villous placental expression of TH receptors (TRs) and the TH transporter MCT8 is increased, whilst the expression of the TH transporter MCT10 is decreased, with severe IUGR. Human cytotrophoblasts (CTs) were isolated from normal (n = 9) and IUGR (n = 5) term placentae (35–40 weeks) and cultured for 90 h. Mean triiodothyronine (T3) uptake by CTs from normal and IUGR placentae was 5% and 6%, respectively. The ''viability'' of CTs (MTT) from IUGR compared to normal placentae was reduced by 20% in the presence of 1 nM T3 ($p<0.01$). Apoptosis (Caspase 3/7 activity) in CTs from IUGR compared to normal placentae was increased by 20% at 1 nM T3. Syncytialisation (HCG secretion between 18 h and 90 h post-culture) increased by 3.5 fold in CTs isolated from IUGR compared to normal placentae in the absence of T3 ($p<0.05$). This response was attenuated with 10 nM T3. Even though CTs from normal and IUGR placentae demonstrate similar efficiency of T3 uptake, they show an altered response to T3 treatment that may be partly attributed to increased TR expression in IUGR. Our data confirm increased apoptosis and syncytialisation in IUGR placentae. Decreased cell ''viability'' and increased apoptosis, but not increased syncytialisation, may be partly mediated by altered TH action within the cytotrophoblast of IUGR placentae, which may adversely affect placental development and contribute to the pathogenesis of IUGR.

2.1 THE COMBINED USE OF TWO POWERFUL PREDICTORS OF PRETERM BIRTH IN HIGH-RISK ASYMPTOMATIC WOMEN

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Objectives: Fetal fibronectin (fFN) testing and transvaginal ultrasound measurement of cervical length (CL) are established as excellent predictors of preterm delivery (PTD). The predictive ability of their combined use in high-risk asymptomatic women is less established.

Methods: All asymptomatic high-risk women that were screened for fFN and CL over a four-month period at St Thomas' Hospital were included for outcome analysis.

Results: 31 pregnant women were recruited; the largest group of high risk asymptomatic women in the literature. 18.3% of women tested positive for fFN. The mean CL was significantly shorter in women who tested positive for fFN (25.5 mm vs 34.1 mm, $p = 0.0019$). Outcome analysis was conducted on 118 women who were not delivered iatrogenically.

Conclusions: The combined use of fFN and CL increases knowledge of the likelihood of PTD which is likely to have a significant impact in clinical practice. Women with +ve fFN but a long cervix may have a greater risk then those with a –ve fFN and a shorter cervix.

Abstract 2.1

	Risk of delivery at $<30^{+0}$ (%)	Risk of delivery at $<34^{+0}$ (%)	Risk of delivery at $<37^{+0}$ (%)
Positive fFN + CL ⩽25 mm	7.14	38.5	46.2
Positive fFN + CL >25 mm	10.0	22.2	25.0
Negative fFN + CL ⩽25 mm	0.0	5.5	11.8
Negative fFN + CL >25 mm	0.0	3.6	10.0

fFN, fetal fibronectin.

2.2 PREVALENCE AND OUTCOME FOR INDIVIDUALS WITH DOWN SYNDROME, 1985–2003

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Background: Down syndrome (trisomy 21) occurs in 1–2 per 1000 births. It is a major cause of severe learning disability and affected individuals often have associated physical morbidities including structural congenital anomalies. We describe changes in the prevalence, outcome and survival of individuals affected by Down syndrome, over a 19-year period.
Methods: All births and terminations with a confirmed diagnosis of Down syndrome and delivered between 1985 and 2003 were identified from the Northern Congenital Abnormality Survey (NorCAS). Office for National Statistics (ONS) death registrations and hospital tracing systems were used to identify the survival status of live born infants. Kaplan-Meier methods were used to examine survival up to age 20 years.
Results: 1101 cases of Down syndrome were notified including 697 (63%) live births and 344 (31%) terminations of pregnancy. Total prevalence was 13.2 per 10 000 births and terminations in 1985–1990, 15.5 in 1991–96, and 16.1 in 1997–2003. The proportion of terminations increased from 16% in 1985–1990 to 39% in 1997–2003 ($p<0.001$). Nearly half (48%) of the live births had at least one additional anomaly. The infant mortality rate was 110 per 1000 live births, with 62% of infant deaths occurring post-neonatally. Survival rates significantly increased over the three successive time periods studied ($p = 0.001$).
Conclusions: The prevalence of Down syndrome is increasing, as anticipated from rising maternal age. Although the proportion resulting in termination of pregnancy has risen, the majority of individuals are born live and their survival has improved over time.

2.3 LOW SALIVA PROGESTERONE CONCENTRATIONS ARE ASSOCIATED WITH SPONTANEOUS EARLY PRETERM LABOUR (BEFORE 34 WEEKS OF GESTATION) IN HIGH-RISK WOMEN

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Background: Identification of women who are at greatest risk of premature labour and delivery remains inaccurate and is still largely based on clinical history. We have previously shown a marked increase in the saliva estriol (E3) concentration and the saliva E3: progesterone ratio before term labour and in symptomatic women who deliver preterm. We have now addressed whether concentrations of saliva E3 and progesterone are abnormal prior to the onset of spontaneous preterm labour.
Methods: Saliva progesterone and E3 concentrations were determined weekly from 24 weeks of gestation in women at increased risk of preterm delivery who were participants in the PREMET trial. Samples were analysed from 28 women with spontaneous onset of labour and delivery before 37 weeks of gestation, and 64 who delivered at term.
Results: Saliva progesterone was significantly lower in the 12 women delivering before 34 weeks than in those delivering later, between 34 and 37 weeks ($p = 0.007$) or at term ($p = 0.009$). The E3 concentration was not different between groups but the E3: progesterone ratio was higher in the women who went in spontaneous labour before 34 weeks ($p = 0.047$). Measurement of saliva progesterone may be of value in the prediction of early preterm labour and in determining which women might benefit from progesterone supplementation.

Supported by Tommy's Charity.

2.4 CAN TWIN PREGNANCY BE SAFELY PROLONGED TO TERM (37 WEEKS GESTATION)

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Background: Intrauterine fetal death (IUFD) occurs more frequently in monochorionic diamniotic (MCDA) compared with dichorionic diamniotic (DCDA) twin pregnancy and may be unpredictable. We examined the incidence of IUFD in twin pregnancy according to chorionicity to help determine optimal timing of routine delivery.
Methods: 10-year retrospective cohort analysis of all consecutive twin deliveries at a single tertiary care centre (1997–2006). Chorionicity was determined by placental examination. Intrauterine growth restriction (IUGR) was defined as birth weight below the 5th percentile for gestational age and significant inter-twin weight discordance as $\geqslant$20%.
Results: Of 276 MCDA (25.3%) and 818 DCDA twin pregnancies (74.7%) $\geqslant$24 weeks delivered, the incidence of IUFD in MCDA twins was three times that in DCDA twins (11/276 (3.9%) vs 11/818 (1.3%) $p<0.001$). Most deaths in MCDA twins (8/11; 72.7%) were associated with twin twin transfusion (TTTS) all occurring before 34 weeks gestation. After 34 weeks, the incidence of IUFD was similar in MCDA and DCDA pregnancies (2/205 (0.97%) vs 6/708 (0.84%) $p = 1$) with a similar prospective risk (<0.5%) in apparently normally grown twins. However, the IUFD risk was greater in pregnancies complicated by growth discordance or IUGR (TTTS excluded) (MCDA 2/82 (2.4%) vs DCDA 5/243 (2.1%); $p = 1$) with the prospective risk of IUFD rising to 4.3 and 2.0 at $\geqslant$36 weeks gestation.
Conclusions: Preterm delivery should be considered in twin pregnancy complicated by growth discordance or IUGR. The benefit of routine preterm delivery, even in MCDA, in normally grown twins is less clear.

2.5 EXTREME OBESITY IN PREGNANCY IN THE UK: PREVALENCE, PREGNANCY COMPLICATIONS AND OUTCOMES

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Background: Obesity is now recognised as an important public health problem globally; recent reports have highlighted obesity as a factor in more than a quarter of maternal deaths in the UK. However, there are no national data on the prevalence of obesity in pregnancy, and in particular few studies have investigated prevalence and outcomes of extreme obesity in pregnancy (body mass index 50 or greater).
Methods: A national cohort study was undertaken using the UK Obstetric Surveillance System (UKOSS) between March 2007 and September 2008.
Results: 100% of UK consultant-led obstetric units contributed data to the study. 1034 extremely obese women were notified over eighteen months, representing an estimated prevalence of 9.3 per 10 000 maternities (95% CI, 8.7 to 9.9). Obese women were more likely to be older, white, multiparous and from routine and manual social groups, and were at higher risk of pregnancy and delivery complications: 11% had gestational diabetes (relative risk (RR) 7.9, 95% CI, 4.0 to 15.6); 10% a preterm delivery (RR 1.5, 95% CI, 1.1 to 2.2); 51% delivered by caesarean section (RR 2.4, 95% CI, 2.1 to 2.9); 2% had a severe haemorrhage (RR 4.2, 95% CI, 1.2 to 14.6); 9% of their infants were macrosomic (RR 4.9 (2.7 to 9.0)). No obese women died but the perinatal mortality rate among their infants was 17/1000 (95% CI, 9 to 30) (RR 2.4, 95% CI, 0.8 to 6.7).
Conclusions: Nearly one in every thousand women delivering in the UK is extremely obese. They have significantly more pregnancy

complications and poorer pregnancy outcomes than comparison women. This has important service implications including the need for additional high weight capacity equipment.

2.6 THE MEDICALISING OF OBESITY DURING PREGNANCY: FORGETTING THE WOMAN INSIDE

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Background: Maternal obesity is a risk factor of major concern to the UK maternity services in relation to the health outcomes of the mother and her baby. Maternity services have responded by managing care based on identifying potential adverse factors. Difficulties monitoring fetal size mean that obese pregnant women have more frequent ultrasound assessments. All obese pregnant women are screened for gestational diabetes and assessed for possible future complicated birth.

The aim of this study was to explore the psychosocial experiences of obese pregnant women.

Methods: A qualitative approach was used to gain an in-depth perspective of these women's experiences. Semi-structured interviews were carried out with 18 obese pregnant women (BMI>35). Data were transcribed verbatim and analysed using the principles of framework analysis.

Results: The findings revealed that obese pregnant women felt that the extra screening processes involved served to ''medicalise'' their pregnancy. The frequent hospital visits were seen as a burden on the woman and her family because of the time and finances involved. Furthermore, the women felt that their emotions and feelings were ignored at the expense of monitoring their physical health and the well being of the fetus. For some women, these feelings were magnified if they had experienced negative interactions with health professionals.

Conclusions: There is a need for health professionals to communicate more effectively the need for extra monitoring in pregnancy if they are obese. Awareness and sensitivity to the women's psychosocial needs will enable women to feel supported throughout pregnancy, birth and the postnatal period.

3.1 MEASURING PLACENTAL TRANSFUSION FOR TERM BIRTHS: WEIGHING BABIES AT BIRTH WITH CORD INTACT

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Background: At birth, blood flow in the umbilical arteries and veins usually continues for a few minutes. The blood transferred to the infant during this time is known as placental transfusion; estimated to be 80–100 ml at term, although these data are from the 1950s and 60s. This study aimed to confirm whether these estimates remain reliable with current management for labour and caesarean section, and to assess the duration of placental transfusion.

Objective: To measure placental transfusion for term vaginal and caesarean births.

Methods: Placental transfusion can be measured by weighing babies before cord clamping: 1 ml of blood weighs 1 g. At birth, the baby was placed onto digital scales, wrapped with towels and a plastic sheet to prevent heat loss. The scales calculated weight every two seconds, with recordings stored electronically. Weighing continued for up to 5 min, the cord was then clamped.

Results: 26 babies were weighed: 13 vaginal births, 13 caesarean. Preliminary analyses was that median volume of placental transfusion was 79 ml (IQR 50–163 ml) for vaginal births and 84 ml (IQR 59–165 ml) for caesarean births. There was no statistical difference in volume of transfusion between the two groups. For most babies placental transfusion was complete by 3 min, but for some it continued for up to 5 min.

Conclusions: Placental transfusion occurs for both vaginal and caesarean births. The volume and duration of transfusion varies considerably. Further research is needed to enhance our understanding of the physiology of placental transfusion and its effects.

3.2 THE RELEASE TRIAL: A RANDOMISED TRIAL OF UMBILICAL VEIN OXYTOCIN FOR RETAINED PLACENTA

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Background: Retained placentas have a high case fatality rate in low resource settings. Umbilical oxytocin injection is a simple procedure that may increase the spontaneous expulsion of the placenta without need for surgeon or anaesthetic.

Methods: Haemodynamically stable women at over 34 weeks gestation with a retained placenta for over 30 minutes were randomly allocated to receive either 50 IU oxytocin or placebo injected into the placenta through an umbilical vein catheter. The primary outcome was need for manual removal of placenta after 30 minutes. The study was funded by WellBeing of Women and the World Health Organization.

Results: 572 women were recruited in 13 sites in the UK, Uganda and Pakistan. The groups were balanced demographically and there was a mean of 65 minutes from delivery to recruitment. There was no difference between the groups in the need for manual removal of placenta (oxytocin 61.3% vs placebo 62.1%, relative risk (RR) 0.98; 95%, CI, 0.87 to 1.12), blood loss over 1000 ml (10.8% vs 9.9%, RR 1.09, 0.67 to 1.76), need for blood transfusion (8.6% vs 11.2%, RR 0.77, 0.46 to 1.26) or any other outcome. Logistic regression showed a significant difference? Is there a word missing here? This sentence needs to be author queried between country effect ($p<0.001$) with umbilical oxytocin being far less successful in the UK than either Uganda or Pakistan.

Conclusion: Umbilical vein oxytocin has no role in the management of retained placenta.

3.3 SUBDURAL, SUBGALEAL AND CEPHALOHAEMATOMA. ARE THESE RESULTS OF OBSTETRIC TRAUMA?

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Purpose: Subdural haematomas in infants are associated with non-accidental head injury and may result in litigation against the medical staff if thought to be a result of mismanagement of the delivery process. We sought to establish the frequency and natural history of subdural haemorrhages and extra cranial bleeds in asymptomatic term neonates, and if the delivery method influenced their occurrence.

Methods: Term babies were imaged within 48 hours of delivery using a 0.2T MRI scanner. Obstetric details were recorded retrospectively from the patients' notes. The incidence of subdural or subgaleal haemorrhage and cephalohaematoma was recorded. Statistical analysis used normal vaginal delivery (NVD) as the baseline.

Results: Imaging from 494 neonates: NVD (n = 269), forceps (n = 35), Ventouse (n = 65), failed Ventouse and subsequent forceps (n = 29), elective caesarean section (n = 49) and emergency caesarean section (n = 47), revealed 38 subdural haemorrhages (7.7%). Of these, 19 were NVD, three were forceps deliveries (odds ratio = 1.23), six were forceps after attempted Ventouse delivery (OR = 3.4; p = 0.02), eight followed Ventouse delivery (OR = 1.96) and one followed emergency caesarean section (OR = 0.38). All had resolved by the four-week rescan with no reoccurrence to date. The

distribution of subgaleal haemorrhage (n = 18) and cephalohaematoma (n = 11) followed that of subdural haemorrhage.
Conclusions: High numbers of clinically silent intracranial and extra cranial haemorrhages occur most frequently in instrumental deliveries and resolve spontaneously without detrimental effects within four weeks. They did not occur together. Subdural haemorrhages after four weeks of age are therefore unlikely to be related to birth injury and traumatic causes must be considered.

3.4 "NORMAL BIRTH MATTERS": THE IMPACT OF AN INTERACTIVE, MULTIMEDIA LEARNING PACKAGE ON MATERNITY STAFF

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Background: This presentation draws on research commissioned by the Department of Health to model, develop and test a learning package for maternity staff to improve support for women who want a normal birth without pharmacological intervention. Interactive workshops and video clips were useful in promoting changes in professional behaviour, and were incorporated into the design of the package.
Methods: Following ethics approval, a study was undertaken of the practices of midwives and doctors working in a National Health Services (NHS) site which has consistently demonstrated high rates of normal birth. Analysis of videoed interviews with women was undertaken and the researchers identified factors that maximised the potential for normal birth. This contributed to developing learning activities and identifying clips for the workshop. The package included an online questionnaire measuring knowledge, attitudes and self-efficacy before and after a half-day interdisciplinary workshop, and a recall session 4–6 weeks later including a communication objective structured clinical examination (OSCE). The learning package was tested in three NHS sites and quantitative and qualitative data were analysed in assessing the impact of the package on participants.
Results: The package demonstrated the potential for maternity staff to learn with, from and about each other to improve collaboration and care. Visual images stimulated learning activities and raised consciousness about ways to support women wishing to have a normal labour and birth. There were small non-significant increases in knowledge. Higher levels of self-efficacy were significantly correlated with higher OSCE performance.
Conclusion: Mandatory training for maternity staff should address opportunities for inter-professional, interactive learning to develop confidence and skills in supporting women to have a positive experience of childbirth.

3.5 MACROPHAGE INFILTRATION OF DECIDUA AND MYOMETRIUM IN RAT MODELS OF PRETERM LABOUR

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Background: Premature birth is the leading cause of neonatal morbidity and mortality. Development of effective treatment is hampered by a lack of mechanistic knowledge. Inflammatory processes are involved in both term and preterm labour (PTL). Leukocytes infiltrate uterine tissues, with highest numbers in decidua; however their role is unknown. In a rat model of PTL induced by RU486, significant myometrial macrophage infiltration was detected. We aimed to characterise decidual macrophage infiltration in rat models of PTL and extreme PTL, and examine relationships between inflammatory events in decidua and myometrium.
Methods: Pregnant rats were treated with: i) RU486 or vehicle on day 15, or ii) RU486 or vehicle on day 19 (n = 4/group), with term pregnancy being 23 days. Full thickness uterine tissues were collected 24 hours after treatment when RU486 groups were in PTL. Multiple sections from each uterus were fixed and paraffin embedded. Macrophages were identified in decidua and myometrium by immunohistochemistry and quantified using image analysis software.
Results: Preliminary analyses show greater macrophage infiltration into decidua in PTL compared to vehicle control at d16 (590 vs 430 / mm^2 of decidua) and d20 (500 vs 210 / mm^2 of decidua). Significantly higher numbers were present in decidua than myometrium (500 vs 270 / mm^2 of uterine tissue) in PTL at d20.
Conclusions: Macrophage infiltration into decidua appears to be an important event in PTL and may be instrumental in inflammatory pathways during labour. These studies validate the rat as a model for PTL, to delineate concurrent events in myometrium and decidua and macrophage involvement.

3.6 A RANDOMISED, DOUBLE-MASKED, PLACEBO-CONTROLLED STUDY OF PROGESTERONE FOR THE PREVENTION OF PRETERM BIRTH IN TWINS (STOPPIT)

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Background: Women with twin pregnancy are at high risk for spontaneous preterm delivery. Progesterone has been found to be effective in preventing preterm birth in high-risk singleton pregnancy.
Methods: Five hundred women with twin pregnancy were recruited from UK National Health Services (NHS) clinics specialising in the management of twin pregnancy. Women were randomised either to daily vaginal progesterone gel 90 mg or placebo, double-masked, and given from 24 weeks of pregnancy for 10 weeks. The primary outcome was death or delivery prior to 34 weeks gestation. (ISRCTN no 35782581.)
Results: Three patients in the progesterone group and three in the placebo group were lost to follow up; thus data from 494 patients were available for the intention-to-treat analysis of the primary outcome. The proportion of women delivering before 34 weeks in the progesterone and the placebo group were 24.7% and 19.4% respectively, the odds ratio of death or delivery prior to 34 weeks of pregnancy was 1.36 (95% CI, 0.89 to 2.09).
Conclusion: Progesterone, administered vaginally, fails to prevent preterm birth in women with twin pregnancy. Our data complement those of Rouse[1] who showed that 17 hydroxyprogesterone caproate, administered intramuscularly, failed to prevent preterm birth in twin pregnancy. Different pathophysiological mechanisms may account for the different efficacy of progesterone in high-risk singleton and in twin pregnancy. Progestogens should not be used to prevent preterm birth in twin pregnancy.

1. **Rouse DJ,** Caritis SN, Peaceman AM, *et al*. A trial of 17 alpha-hydroxyprogesterone caproate to prevent prematurity in twins. *N Engl J Med* 2007;**357**:454–61.

4.1 BIOLOGICAL ACTIVITY OF VASCULAR ENDOTHELIAL GROWTH FACTOR IN PRE-ECLAMPSIA

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The microvasculature of a woman with pre-eclampsia is in a state of increased microvascular permeability, which leads to the characteristic clinical findings of maternal oedema and proteinuria. The vascular endothelial growth factor (VEGF) family increases vascular permeability via activation of VEGF receptors -1 and -2,

and is highly expressed in the plasma of pre-eclamptic women. This study aimed to determine if this family of molecules is responsible for the pro-permeability of pre-eclampsia, and if so to identify the specific VEGF isoforms responsible for this permeability rise. Plasma from pre-eclamptic (n = 17) and normotensive (n = 10) pregnant women was perfused into frog mesenteric microvessels, and the subsequent change in microvascular permeability measured using the Landis-Michel Micro-occlusion technique. This technique involves the cannulation and perfusion of microscopic vessels with pre-eclamptic plasma, occluding the vessel downstream of the cannula, and measuring the filtration across the vessel wall. Pre-eclamptic but not normotensive plasma resulted in an average 5.25 ± 0.8 fold acute increase in vascular permeability ($p = 0.0003$). This rise in permeability could be blocked by incubation of plasma with bevacizumab, an antibody to VEGF (n = 7, $p = 0012$), and by VEGF receptor inhibition. This increase was further inhibited by SU5416 at doses specific to VEGF receptor-1, but not by the VEGF receptor-2 inhibitor, ZM323881. Incubation of pre-eclamptic plasma with an inhibitory monoclonal antibody specific for the $VEGF_{165}b$ isoform inhibited the rise in vascular permeability (n = 6, $p<0.01$). These findings suggest that $VEGF_{165}b$ may be involved in the increased vascular permeability of pre-eclampsia.

4.2 FIRST TRIMESTER MARKERS FOR THE PREDICTION OF PRE-ECLAMPSIA IN WOMEN WITH A PRIORI HIGH RISK

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Objective: To evaluate the combination of first trimester placental protein 13 (PP13), uterine artery Doppler and pulse wave analysis for the prediction of pre-eclampsia in women with a priori high-risk.
Methods: This was a nested case control study. Women between 11^{+0} and 13^{+6} weeks' gestation at increased risk of developing pre-eclampsia were recruited. Uterine artery Doppler and pulse wave analysis were measured, and venous samples assayed for PP13 using ELISA. Multiples of median (MoM) were calculated and adjusted for BMI, smoking, ethnicity, maternal age and parity. For each case of pre-eclampsia (n = 42), five controls were randomly selected from the study group. PP13 levels, mean pulsatility index (PI) and augmentation index at heart rate of 75/min (AIx-75) were compared between women who developed pre-eclampsia and controls using the Wilcoxon rank sum test. Sensitivity and specificities were derived from receiver operating characteristic curves.
Results: Compared with controls, women who developed pre-eclampsia had significantly lower PP13, higher mean PI and higher AIx-75 ($p<0.001$). For a fixed false positive rate of 10%, the best detection rate for all pre-eclampsia (85.7%, 95% CI, 71.5 to 94.6%) and pre-eclampsia before 34 weeks' gestation (92.9%, 95% CI, 66.1 to 99.8%) was achieved by a combination of PP13, mean PI and AIx-75. The equivalent detection rates for the combination of PP13 and AIx-75 were 81.0% (95% CI, 65.9 to 91.4%) and 85.7% (95% CI, 57.2 to 98.2%).
Conclusions: The combination of first trimester PP13 and pulse wave analysis achieved clinically useful prediction of pre-eclampsia in women at increased a priori risk. The addition of mean PI did not significantly improve prediction of pre-eclampsia.

4.3 MATERNAL PLASMA FATTY ACID COMPOSITION AND PREGNANCY OUTCOME IN PREGNANT ADOLESCENTS: THE ABOUT TEENAGE EATING STUDY

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Background: Adolescents are at increased risk of adverse pregnancy outcome, including small-for-gestational age (SGA) babies and preterm birth. A lower intake of n-3 long-chain polyunsaturated fatty acids (LCP) may reduce gestational duration. Since adolescents have low intakes of oily fish, the main source of n-3 LCP in the UK diet, we prospectively assessed maternal plasma fatty acid composition in pregnant adolescents from London and Manchester and determined associations with pregnancy outcome.
Methods: 500 subjects, aged 14-18 years, were recruited at $\leqslant 20$ weeks' gestation. Third trimester blood samples were provided by 291 participants and plasma fatty acid composition measured by gas-liquid chromatography. Frequency of oily fish consumption was assessed by eating behaviour questionnaire. SGA birth was assessed by customised centiles. Differences in plasma fatty acids between pregnancy outcomes were determined by multiple logistic regression, adjusting for confounding variables. Principal components analysis was used to derive patterns in fatty acid profiles, which were compared with pregnancy outcome.
Results: 16% of infants were born SGA and 9.9% were preterm. Plasma n-3 LCP did not differ significantly in SGA cases, as compared with non-SGA cases, although dihomo-γ-linolenic acid (DGLA) was lower ($p = 0.033$; adjusted value). Plasma fatty acid composition did not differ between mothers delivering term and preterm infants, and no association was found with gestational duration. The "n-3 LCP" principal component was not associated with pregnancy outcome.
Conclusions: A lower DGLA concentration is associated with greater risk of SGA birth. Plasma n-3 LCP concentrations are not associated with adverse pregnancy outcome in UK adolescents.

4.4 THE GESTATION-SPECIFIC RISK AND PREDICTORS OF ANTEPARTUM STILLBIRTH IN BABIES OF WOMEN WITH TYPE 1 AND TYPE 2 DIABETES IN ENGLAND, WALES AND NORTHERN IRELAND: A POPULATION BASED STUDY

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Objectives: To investigate the gestation-specific risk, and the predictors, of antepartum stillbirth (APSB) in babies of women with type 1 (T1DM) and type 2 diabetes (T2DM).
Design: National population-based cohort.
Participants: 2130 women from 231 maternity units with T1DM and T2DM, delivering a singleton, normally-formed baby at 24 or more weeks' gestation, from March 2002 to February 2003.
Statistical Methods: Life-tables, Cox and logistic regression models.
Results: APSB occurred in 2.3% of pregnancies. Planned delivery occurred in 81% of pregnancies, of which 71% were after 36 weeks' gestation. The survival distribution among babies of T1DM pregnancies was similar to T2DM pregnancies ($p = 0.85$). The hazard rate (HR), ie risk of APSB per week in 1000 continuing pregnancies, increased with advancing gestation from 34 weeks to 38 weeks (HR 2.8 and 8.7, respectively). The predictors of APSB included birth weight below third percentile (OR 35.3, 95% CI, 10.3 to 120.8) and HbA1c above 7.0% (OR 9.2, 95% CI, 3.0 to 27.6). In women with HbA1c above 7%, the HR at 34 weeks and 38 weeks was 10.5 and 26, respectively and the neonatal admission rate to intensive care unit (ICU) was 28% when compared to 16% in babies of women with HbA1c $\leqslant 7\%$.
Conclusion: A routine elective delivery at 34 weeks' gestation in women with HbA1c above 7% could prevent 30 APSB per 1000 pregnancies at or beyond this gestation but the relative risk of neonatal admission to ICU was 4.7 (95% CI, 3.3 to 6.7) when compared to elective delivery after 36 weeks' gestation.

4.5 A PROSPECTIVE STUDY OF HIGHLY SENSITIVE C-REACTIVE PROTEIN THROUGHOUT PREGNANCY AND POSTPARTUM IN WOMEN WHO DEVELOPED PRE-ECLAMPSIA AND PREGNANCY-INDUCED HYPERTENSION

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Background: Healthy pregnancy is a pro-inflammatory state in which C-reactive protein (CRP) is thought to predict pre-eclampsia. However, studies have been cross-sectional and mostly measured CRP rather than highly sensitive CRP (hsCRP).
Objective: To prospectively assess levels of hsCRP throughout pregnancy until 3 months postpartum.
Methods: 135 pregnant, non-smoking women were recruited from early pregnancy and blood samples were taken at 6 weekly intervals until 3 months' postpartum. Highly sensitive CRP was measured using an automated analyser (Roche Diagnostics). Data were analysed using ANOVA and were corrected for multiple comparisons.
Results: Pre-eclampsia developed in 18/135 and pregnancy-induced hypertension (PIH) in 10/135 women. In the first trimester, serum hsCRP levels were similar in women who later developed pre-eclampsia (4.7 ± 1.0 mg/L) and those who had a normotensive pregnancy (4.5 ± 0.5 mg/L) and remained similar throughout pregnancy. Postpartum, hsCRP levels fell to 2.3 ± 0.5 mg/L in women who had pre-eclampsia and to 2.0 ± 0.3 mg/L in normotensive subjects ($p<0.001$). In the first trimester, hsCRP levels appeared higher in women who developed PIH (5.7 ± 1.3 mg/L) and remained higher postpartum (3.3 ± 1.0 mg/L).
Conclusions: The similar rise in maternal serum hsCRP in normotensive and pre-eclamptic pregnancies suggests that inflammation plays a role in sustaining healthy pregnancy, but not in the aetiology of pre-eclampsia. The elevated hsCRP seen in women who had PIH suggests a possible role for inflammation in the aetiology of this condition.

4.6 DO MATERNAL CARDIAC STRUCTURAL ABNORMALITIES PREDISPOSE TO HIGH-RESISTANCE UTERINE ARTERY DOPPLER INDICES?

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Objective: To compare the prevalence of previously undiagnosed cardiac defects in women with normal and high resistance indices at mid-trimester uterine artery Doppler screening.
Methods: Maternal echocardiography was undertaken in pregnant women after uterine artery Doppler screening for pre-eclampsia at 21–23 weeks gestation. Women with a mean uterine artery pulsatility index above 95th centile (1.25) for the local population (multi-ethnic, socially diverse and migrant) were considered to have a high resistance uteroplacental blood flow indices. The prevalence of cardiac structural defects in these women was recorded.
Results: A total of 210 women consented to have maternal echocardiography: 86 with high resistance and 124 with normal resistance uterine artery blood flow indices. There were five previously undiagnosed, functionally significant cardiac defects in this cohort, all in the high-resistance uterine blood flow group ($p<0.05$). The newly diagnosed cardiac defects included: large atrio-septal defects with unidirectional shunt, right/left heart disproportion and pulmonary hypertension ($n = 2$), mitral valve disease possible secondary to rheumatic heart disease ($n = 2$) and bicuspid aortic vale with aortic regurgitation ($n = 1$) AU: Should this be bicuspid aortic valve with aortic regurgitation?.
Conclusion: The prevalence of previously undiscovered maternal cardiac structural malformations appears significantly increased in women with high mid-trimester uterine artery Doppler resistance indices. This observation should be confirmed in a larger series of patients because it has important consequences for medical practice and the long-term care provided to these patients.